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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,180	03/20/2006	Blas Cerda	NEN-23002/16	2257

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EXAMINER	
MARTIN, PAUL C	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,180	CERDA, BLAS	
	Examiner	Art Unit	
	Paul C. Martin	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 16-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 16-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-11 and 16-29 are pending in this Application and were examined on their merits.

The objection to the Drawings for including reference characters not mentioned in the description has been withdrawn due to the Applicant's amendments to the Claims filed 11/02/07.

The objection to the Specification for improper use of trademarks has been withdrawn because the Applicant's arguments regarding the placing of the terms in all caps were found to be persuasive.

The rejection of pending Claims 1, 5-11 and 17-29 under 35 U.S.C. § 103(a) as being unpatentable over Gerber *et al.* (2001) in view of Roe *et al.* (1999) and Guerra-Giraldez *et al.* (2002) has been withdrawn due to the Applicant's amendments to the Claims filed 11/02/07.

The rejection of pending Claims 1-11 and 16-29 under 35 U.S.C. § 103(a) as being unpatentable over Gerber *et al.* (2001) in view of Roe *et al.* (1999) and Guerra-Giraldez *et al.* (2002) and further in view of Chace *et al.* (2001) has been withdrawn due to the Applicant's amendments to the Claims filed 11/02/07.

Double Patenting

The provisional rejection of pending Claims 1-11 and 16-27 under 35 U.S.C. § 101 as claiming the same invention as that of Claims 1-28, 45-47 and 54-57 of copending Application No. 10/539273 is maintained for reasons of record set forth in the prior action.

The provisional rejection of pending Claims 1-8, 10, 19-21, 23, 24 and 27 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-5, 7, 12, 14-18 and 20-26 of copending Application No. 10/652,732 is maintained for reasons of record set forth in the prior action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 and 16-29 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the detection of the metabolic disorder Biotinidase Deficiency in an individual, does not reasonably provide enablement for the detection of any metabolic disorder in an indivdual. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands.,* 58 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention.

"Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404).

The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Nature of the Invention:

The instant invention is directed toward the detection of any metabolic disorder in an individual comprising the detection of the presence or amount of one or more metabolic analytes and the presence or amount of at least one enzyme product.

Presence or Absence of Working Examples:

The sole working example is directed to the simultaneous determination of the amount of biotinidase (enzyme)/biocytin(substrate) reaction product (presumably biotin and/or lysine) and the endogenous metabolic analytes acylcarnitines and α-amino acids.

Amount of Direction or Guidance presented:

The disclosure broadly defines a "metabolic disorder" as any condition that interferes with normal creation or destruction of biological molecules that regulate health. However, the claims and teachings of the instant disclosure are directed only to those specific metabolic disorders having both detectable metabolic analytes and enzymatic reaction products, such as Biotinidase Deficiency. The Applicants disclosure does not teach or suggest how one of ordinary skill in the art will detect any other metabolic disorder in an individual if the metabolic disorder is not characterized by the metabolically indicative enzyme biotinidase and metabolic analyte biotin

Breadth of the Claims:

The claims are broadly drawn to the detection of any metabolic disorder in an individual comprising the detection of the presence or amount of one or more unspecified metabolic analytes and the presence or amount of at least one unspecified enzyme product (biotin?).

The State of the Prior Art:

As stated above, the instant invention is drawn to the detection of any metabolic disorder relying upon the detection of the presence or amount of one or more unspecified metabolic analytes and the presence or amount of at least one unspecified enzyme product (biotin?).

However, it is known in the Art that certain metabolic disorders are not characterized by both metabolic analytes and enzyme-mediated reaction products.

For example, Gahl *et al.* teaches the metabolic disorder cystinosis, a lysosomal storage disease that results from the impaired transport of cystine, usually through a mutation in the gene for cystinosin (Pg. 114, Column 2, Lines 3-4 and Pg. 115, Column 1, Lines 25). The Merck Manual Home Index teaches that the metabolic disorder Alkalosis, excessive blood alkalinity is caused by either a loss of acid from the blood or an overabundance of bicarbonate in the blood. Neither of these two metabolic disorders are characterized by both metabolically indicative enzymes and analytes and thus could not be detected in an individual using the instant invention.

For all of the reasons above, the instant disclosure does not reasonably provide enablement for the detection of any metabolic disorder in an individual, or any metabolic disorder that does not have both metabolically indicative enzymes and analytes. Therefore the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 16-29 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the limitation "wherein one or more protease inhibitors are present" in lines 8 and 9. There is insufficient antecedent basis for this limitation in the claim. I.e., there is no step wherein protease inhibitors are added to the reaction mixture or contacting a sample with protease inhibitors. Claims 2-11 and 16-29 are rejected as being dependent upon rejected Claim 1.

Claims 1-11 and 16-29 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 in step (a) contains the method steps of contacting a sample comprising biotinidase and one or more metabolic analytes with the biotinidase substrate biocytin to generate a product. Step (b) then contains the step of contacting the reaction admixture with a reagent that inhibits biotinidase to act on biocytin, however the biotinidase in the sample of step (a) has already contacted and reacted with the biocytin substrate in step (a). It is unclear how any inhibitor will prevent this reaction after the fact.

Further, step (a) states that the sample comprises one or more metabolic analytes and biotinidase which is contacted with the biotinidase substrate biocytin (and presumably generates a reaction product), while in step (c) contains a step of determining the presence or amount of the one or more metabolic analytes and at least one product is correlated with the presence or absence of a metabolic disorder. If the conditions of step (a) are performed, *every* test sample *every* time will contain one or more metabolic analytes and at least one product and therefore it is unclear how any correlation will take place. Claims 2-11 and 16-29 are rejected as being dependent upon rejected Claim 1.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

12/27/07

Jon Weber
Supervisory Patent Examiner